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FORECAST PARKINSON DISEASE PROGRESSION TO BETTER SELECT PATIENTS INTO TRIALS

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Objectives Subject recruitement is a burden that hampers clinical trials, especially in neurodegenerative diseases inducing long-term and subtle worsening of abilities. Better selecting them allows to reduce their required number - or conversely to improve the proven effect size.

Methods We extracted one-year separated visits in PPMI to model the placebo arm. For each patient, we derive a treated counterpart by applying an individual treatment effect calibrated so to get an effect size that correspond to a 4 point MDS-UPDRS II + III improvement and from which we derive a required sample size. Then, thanks to individual outcome predictions [Schiratti et al, 201] from which we derive a individual ratio of MDS-UPDRS II + III change, we select a subset of patients that minimizes the sample size for the previous effect size. The optimal ratio value is estimated on 80% of the PPMI patients and tested on the last 20%. We then test this ratio on DIGPD. The operations are bootstrapped 100 times on 50% of the data.

Results By selecting patients whose one-year MDS-UPDRS II+III ratio of predicted change is of 0.078 and for 0.4 of effect size, the number of patients needed to show a 0.4 effect size is reduced by 45±(11.4)SD% (resp. 55±(7.6)SD%) on the test set (resp. DIGPD evaluation).

Conclusions The use of our prediction model can concretly improve clinical trials on Parkinson's disease by helping to better select patients and thus reduce the cohort size for a fixed treatment effect size.

References

[Schiratti et al, 201] Schiratti J-B, Allassonniere S, Colliot O, Durrleman S. *A Bayesian mixed-effects model to learn trajectories of changes from repeated manifold-valued observations*. In *Journal of Machine Learning Research (JMLR)* 18(1):4840-4872. 2017.

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